Clustering of Seizures in Alcohol-Related Seizures - A Study from a Tertiary Care Center in South India

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ABSTRACT

Introduction: Seizures are one of the commonest neurological emergency encountered in an alcoholic. While most studies deal with seizures in the setting of alcohol withdrawal,alcohol is also known to precipitate underlying IGE syndromes. Aim: aim of this study is to analyse the relationship between patterns of alcohol consumption and epilepsy with focus on clinic etiological profile of the patients.

Materials and methods: This was a cross sectional observational study conducted in a tertiary care centre in Tamil Nadu.100 consecutive patients were included in the study after excluding patients with a known seizure disorder and another proximate cause of seizure such as CVT, intracranial haemorrhage.

Results: All 100 patients were male with a mean age of 51.6 (10.1) years. Mean time interval between prior alcohol intakes to the first seizure was 18 h. Mean duration of alcohol use was 19.95 (10.172) years. 91%(91) patients had generalized tonic clonic seizures (GTCS) while 9%(9) patients had focal onset seizures.45 % of patients showed clustering of seizures and it was significantly associated with total duration of alcohol consumption (p=0.049),recent change in drinking patterns (p=0.026),presence of withdrawal symptoms at admission (p=0.031)and previous history of alcohol with drawl seizures (p=.001).

Conclusion: Pattern of alcohol consumption has an important role in alcohol related seizures .It also has a strong association with severity of seizure as evidenced by association with clustering.Focal seizures at presentation merits a detailed evaluation for structural lesions.

Keywords :Seizures.Alcohol related seizures.Clustering

INTRODUCTION

Epilepsy is one of the most typical neurological emergencies with an annual incidence of 70 per 100,000 people.[1] Alcohol is an important risk factor and has a strong proven relationship with epilepsy.Most studies done related to this topic have focused on epilepsy occurring in the background of alcohol withdrawal state.However recent research has unearthed alcohol as having an independent effect on kindling of seizures, especially in the setting of unprovoked seizures in an alcoholic.[2] Alcohol is also known to unmask underlying IGE syndromes by reducing seizure threshold and a late-onset ARS might be the first presentation of the same.[3] In contrast,the reverse is also true in that events labelled as unprovoked seizures often turn out to be AWS on detailed history taking. Alcohol consumption is also known to predispose to vascular events, especially CVT.

Another pertinent question on this subject was the patient characteristics of an alcoholic rendering them susceptible to epilepsy, given that only a small minority of alcoholics have a seizure in their lifetime. This study aims to analyze the relationship between patterns of alcohol consumption and clustering of seizures at presentation with focus on the clinical etiological profile of the patients.

MATERIAL AND METHODS

100 patients were selected who presented to neurology emergency, OPD or wards of Thanjavur government medical college, Thanjavur, Tamil Nadu with a history of alcohol related seizures from December 2019 to December 2020. after written informed consent and Internal ethics committee approval relevant details regarding alcohol use and seizure history from participants were documented.A detailed history of alcohol consumption pattern was taken along with history suggestive of clustering.Clustering was defined as three or more seizures within 24 hours with complete neurological recovery in between,and their epidemiological data was analysed separately to ascertain the probable risk for serial seizures. AUDIT [Alcohol use disorders identification test] score was used to identify patients with alcoholism and to ascertain level of hazardous drinking.Patients with a proven alternate cause of seizures such as cerebral venous thrombosis, known cases of epilepsy etc were excluded.Apart from detailed neurological examination, routine laboratory tests were done.CT brain was done in all patients.MRI was done in 10 patients who had focal onset seizures.Those patients whose general condition deemed them stable for routine EEG underwent an EEG in clarity 24 channel EEG machine with scalp electrodes in 10-20 system.[5]

Statistical analysis was done using SPSS. Continuous variables were analysed by independent student t test and categorical variables were analysed by chi square test and Fischer's exact test.P value of <0.05 was considered statistically significant

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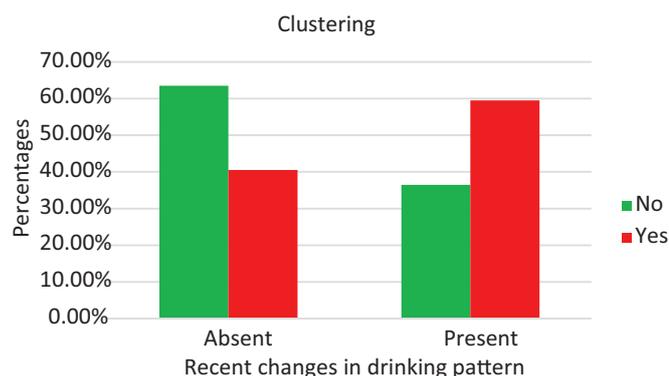| Patient characteristics	
Age	51.6 (10.1)
Gender	100 males
Mean duration of alcohol intake	19.95(10.172)
Type of alcohol	Brandy (52), rum(32), beer (9), whisky (7)
Mean daily intake in past 1 month	141.3 gm
Mean AUDIT score	21.72
Mean intake in bout before seizures	249.4 gm
Average number of seizures	1.84
Mean time between alcohol intake and to seizure	18 hours
Recent increase in drinking frequency or change in pattern	37 % (37)
Clustering in the current episode	45%(45)
Semiology of seizures	GTCS-91 focal onset with secondary tonic clonic-8 Focal onset with impaired awareness.
history of delirium tremens in the past	6
Presence of withdrawal symptoms before seizures	74 %(74)
Presence of withdrawal seizures on the past	14% (14)
History of seizures in first degree relative	5 %(5)
History of febrile seizures	4%(4)
CT scan findings	Generalised atrophy -(22)
MRI findings	Focal gliosis -2 frontal lobe cortical dysplasia -1
EEG	Generalised delta slowing -3.No IEDS
Table-1:	

Figure-1: Association between clustering and recent change in drinking patterns

RESULTS

All 100 consecutive patients enrolled for the study were males. The patient characteristics are provided in table 1.

The average age of patients was 51.6 (10.1)The mean AUDIT score was 21.72 indicating a severe degree of alcohol related problem amounting to alcohol dependence. Mean duration of alcohol use was 19.95 (10.172) years with 44% patients using alcohol for more than 20 years. Nearly, 52 % patients were in the habit of consuming brandy. Mean daily intake in the month prior to seizure was 141.3 gm. The mean alcohol intake in the bout before seizure was 294.4g. Mean number of seizures per patient during the current episode was 1.84. Clustering defined as three or more seizures at presentation occurred in 64 patients (64%). Mean time interval between prior alcohol intakes to the first seizure was 18 h. 91% patients had generalized tonic clonic seizures (GTCS) 9% of patients had semiology suggestive of focal onset seizures.

There were no cases of status epilpeticus. 5 (5%) patients reported epilepsy in a first degree relative while 4 (4%) had a history of febrile seizures. 74% patients had withdrawal symptoms at the time of first seizure.15 patients had just one seizure and none had any withdrawal symptoms even after their sole seizure.

There were 9 patients who consumed beer as a primary drink. They consumed 349.13 grams of alcohol in the last bout prior to the seizure which was higher than the mean consumption 294.4 gm ;out of which 4 patients had hyponatremia.

Clustering of seizures as defined in our study as occurrence of 3 or more seizures within 24 hours was found in 45 %(45) of patients.It was found to have a significant association with total duration of alcohol consumption (p=0.049),recent change in drinking patterns (p=0.026),presence of withdrawal symptoms at admission (p=0.031)and previous history of alcohol with drawl seizures (p=.001).relationship between generalised trophy in CT brain was assessed in association with duration of alcohol intake and clustering,no statistical significance was found.

89 patients presented with seizures between 6 and 48 h of alcohol use and can be considered as having withdrawal seizures. 11 patients had seizures between 0-6 h of alcohol intake. 10 patients out of the 11 had no withdrawal symptoms. 22 patients (22%) had non-specific generalized cortical atrophy on CT scan of the brain. Eighteen patients who had cortical atrophy presented with clustering of seizures. MRI of the brain was done in 10 patients with semiology suggestive of partial seizures. 1 patient had MRI suggestive of focal cortical dysplasia in the right frontal lobe. 2 patients had focal gliosis secondary to previous unknown vascular insults.all three of them had presented before 6 hours from last drink.Scalp EEG recording was done in 25 patients. 3

patients had generalised slowing,remaining EEG s were found to be normal.

DISCUSSION

Alcohol is one of the five most important risk factors for global disease and disability burden.[6] Its association with epilepsy has been shown from various animal models and metanalyses.[2] A significant number of patients presenting to emergency services with history of seizures have history of alcohol consumption.[7] Mechanisms underlying production of seizures in ARS are now being attributed to a kindling phenomenon involving the inferior colliculus of brainstem.[8] Repeated attempts at detoxification has been found to be associated with reducing the seizure threshold for the epileptogenic state triggered by alcohol withdrawal.[9] Molecular mechanisms include alterations in GABA receptor function and glutamatergic over activity induced by long standing ethanol use.[9]

The elicitation of drinking pattern in our patients showed a high incidence of drinking problem in our society. The mean intake of alcohol in the month prior to seizure was around six drinks per day with mean AUDIT scores of 21.72. 70% patients had AUDIT scores more than 20,which is the recommended cut off for mandatory de addiction referral.[10] It was also noted that the intake of alcohol in the bout before the seizure was significantly higher than the mean for the past 1 month indicating the potential role of alcohol in inducing these seizures.

In our study 11 patients had seizures within 6 hours of alcohol intake. They neither had alcohol intoxication on clinical examination and on follow up they did not develop withdrawal symptoms. 3 of them presented with focal onset seizures with secondary generalisation.EEG was normal in two and showed focal frontal slowing in in one.MRI was found to be abnormal in all three with evidence of focal gliosis in two and cortical dysplasia of right frontal lobe in one.This is a pointer towards the utility of MRI scan in those with focal onset or early onset (less than 6 hours from last drink) seizures.There were no cases of status epilepticus.

Family history of seizures was obtained in 5 patients in comparison to 8 and 25 in two similar Indian series.[11-12] History of febrile seizures in childhood was obtained in 4 patients similar to 3 patients in a study by Sandeep et al[12]

There is a well established relationship between total duration of alcohol intake and epilepsy,which was also reflected in our study with a statistically significant association between presence of clustering and duration of alcohol intake. However, in contrast to the study by Sandeep et al we did not get significant association between presence of cerebral atrophy in CT brain and duration of alcohol intake.

Clustering is one of the more critical prestation of seizures and may portend a status epilepticus.[13] Previous studies have noted higher association of clustering with acute symptomatic seizures than epileptic syndromes.[14] In our study clustering was found to have a significant association with recent change in drinking pattern as reported by patients and presence of withdrawal symptoms,which is also similar

to an observation made another Indian study.[12] We also had a higher number of patients with clustering compared to other Indian studies.Most studies analysing the risk factors of seizure clustering have failed to examine the relationship with alcohol.[15] It was also noted that of the three patients with beer potomania,all three had clustering.

These findings prove that prolonged alcohol use and neurochemical changes accompanying tolerance have a definite role in triggering an epileptogenic state.

We could not find any evidence of underlying IGE syndrome in our patients when compared to other Indian studies mentioned earlier.However this may be because of the limited number of EEGs we did in view of the ongoing COVID pandemic.

CONCLUSION

Pattern of alcohol consumption has an important role in triggering AWS.It also has a strong association with severity of seizure as evidenced by association with clustering. If untreated these cases may have progressed to status epilepticus.Causes for symptomatic seizures must be thoroughly elucidated in patients with partial onset seizures to rule of focal pathology.MRI imaging of these cases has a higher yield of diagnosis. EEG in patients with alcohol withdrawal seizures is of limited value however it may be helpful in an underlying syndrome or focal onset which is missed in preliminary investigation.Lastly the alarmingly high rate of hazardous alcohol use in our society needs addressal by a multimodal approach.

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